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CASE REPORT

Severe dermatomyositis with pronounced generalized subcutaneous edema and dysphagia: A rare manifestation of a highly active disease

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ABSTRACT

Severe subcutaneous edema is rare in dermatomyositis (DM). Such patients usually have a highly active disease, which requires aggressive treatment. To date, there are 14 reported cases of generalized edema secondary to adult DM. We described a severe case of DM manifesting generalized edema, oropharyngeal dysphagia, and dysarthria. A 44-year-old female presented with a typical rash of DM, proximal muscle weakness, and marked swelling of the limbs and face. The findings in the skin biopsy, muscle enzymes, and electromyography were consistent with DM. No internal malignancy was detected. After a brief initial response to oral dexamethasone, the patient experienced a sudden worsening of muscle weakness with dysarthria and an inability to swallow even saliva. A magnetic resonance imaging study revealed edema of the subcutaneous tissue and muscles. The symptoms improved gradually in 2 months after intravenous pulse corticosteroid therapy. Generalized subcutaneous edema is a very rare manifestation of DM that can occur as a presenting symptom. It appears to be a hallmark of a severe DM that requires prompt and aggressive treatment. Additional cases are needed to establish guidelines for treatment of this rare variant.

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Introduction

Dermatomyositis (DM) is an autoimmune disorder that causes proximal muscle weakness and manifests with several characteristic skin rashes, including heliotrope periorbital rash, Gottron's papules, Shawl sign, V sign, and periungual telangiectasia. Diagnosis of DM relies on typical clinical manifestations, elevation of serum muscle enzyme levels, and a characteristic electromyographic (EMG) pattern. Periorbital edema is commonly seen in inflammatory myopathy, but generalized edema is an unusual presenting feature. To date, there are 14 reported cases of generalized edema secondary to adult DM.^{1–10} Cases of juvenile DM with anasarca were also reported.^{11–14} Such patients usually have a highly active disease with pronounced muscle weakness and dysphagia, which require aggressive treatment. We report a female patient who had acute edematous DM, with a relatively good initial response to oral dexamethasone. After a brief improvement, she experienced a sudden worsening of muscle weakness, with

oropharyngeal dysphagia and dysarthria, which improved gradually in 2 months after intravenous pulse corticosteroid therapy.

Case Report

A 44-year-old female without past history of renal or heart disease, presented with a 2 month history of erythematous maculopapular skin rash over the face, V-neck, back, and all extremities. She also experienced proximal muscle weakness in association with generalized swelling for 2 weeks prior to admission. The patient noted a body weight gain of 7 kg in 4 weeks (from 68 kg to 75 kg). Physical examination revealed Gottron's papules on the dorsal hands ([Figure 1](#)), a periorbital heliotrope rash, and a generalized non-pitting edema, which was most pronounced over the face and upper limbs, especially the hands. A neurological examination showed decreased muscle power in her shoulder and pelvic girdles. Laboratory evaluations revealed a white blood cell count of 6700/mm³, a hemoglobin level of 10.8 g/dL, a platelet count of 319,000/mm³, an elevated muscle enzyme creatine kinase of 992 IU/L, aspartate transaminase (AST) of 106 U/L, and alanine transaminase (ALT) of 50 U/L. Albumin was 2.8 g/dL, but there was no proteinuria on urinalysis. Renal and thyroid function test results were unremarkable. Circulating antinuclear antibodies were weakly positive (1:80), but anti-Jo-1 antibody, anti-Ro/La antibody, anti-ribonucleoprotein antibody, anti-Smith antibody, and

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Figure 1 Generalized edema in a 44-year-old woman with acute dermatomyositis. Note diffuse swelling of the hands and fingers with Gottron's papules and prominent periungual erythema.

anticardiolipin antibody were all negative. The chest radiography, electrocardiography, and sonography of the abdomen were unremarkable. Sonography of the bilateral upper extremities showed diffuse edema of subcutaneous and fascia layers (Figure 2). Histological examination of a skin lesion over the right postauricular area showed vacuolar interface dermatitis compatible with DM. The patient refused to undergo EMG. With the exclusion of other causes for limb edema, a diagnosis of DM with severe subcutaneous edema was made. She was then treated with oral dexamethasone 6 mg/day, which resulted in an improvement in muscle weakness and edema in 9 days, and markedly decreased muscle enzymes. A search for internal malignancy produced negative results. The patient was discharged on oral dexamethasone 6 mg/day.

After 2 weeks, she experienced a sudden worsening of muscle weakness, with elevation of muscle enzyme levels, in association with dysarthria and an inability to swallow even her saliva. Magnetic resonance imaging from the nasopharynx to the bilateral

upper limbs showed edematous changes of hyperintensity at the muscles, subcutaneous regions, and intermuscular fasciae (Figure 3). EMG revealed findings consistent with inflammatory myopathy. Intravenous methylprednisolone 80 mg/day (40 mg bid) was initiated, but the clinical response was slow. Her dysphagia remained severe, and she was placed on a nasogastric tube for feeding. Myasthenia gravis was excluded by normal responses in a repetitive nerve stimulation test and a negative neostigmine diagnostic test.

Due to elevated hepatic enzymes (AST/ALT = 138/85 U/L), methotrexate was not used as an alternative. After administering intravenous methylprednisolone 80 mg/day for 7 days, pulse intravenous methylprednisolone (500 mg/day) was administered for 5 days. This was followed by intravenous methylprednisolone 80 mg/day for another 11 days and then oral prednisolone 90 mg/day for 4 days prior to discharge. Despite a marked decline in serum muscle enzyme levels and improvement of subcutaneous edema, there was no appreciable clinical response in dysphagia and proximal muscle strength. The patient was then transferred to the neurology ward for further evaluation and treatment. Non-enhanced brain computed tomography was performed and found no definite intracranial abnormality, which supported the theory that the dysarthria and poor soft palate elevation was a manifestation of DM activity. The patient later developed right lung pneumonia with fever and productive coughs. After the infection was treated with parenteral antibiotics, she was discharged on oral prednisolone 90 mg/day, with a slight improvement of proximal muscle weakness and dysphagia (the nasogastric tube was still in place). One month after discharge, the nasogastric tube was successfully removed, with the resumption of a normal diet. Currently, she is on prednisolone (40 mg/day), and her DM is improving both biochemically and clinically.

Discussion

We described a severe case of DM manifesting marked proximal muscle weakness in association with a generalized non-pitting edema (most pronounced over the face and upper limbs), and oropharyngeal dysphagia. The most common causes of anasarca are hypoalbuminemia, heart failure, cirrhosis, and renal insufficiency.⁵ Other causes may be related to deep vein thrombosis, hypothyroidism, medications, and malignancy.⁶ Despite an extensive

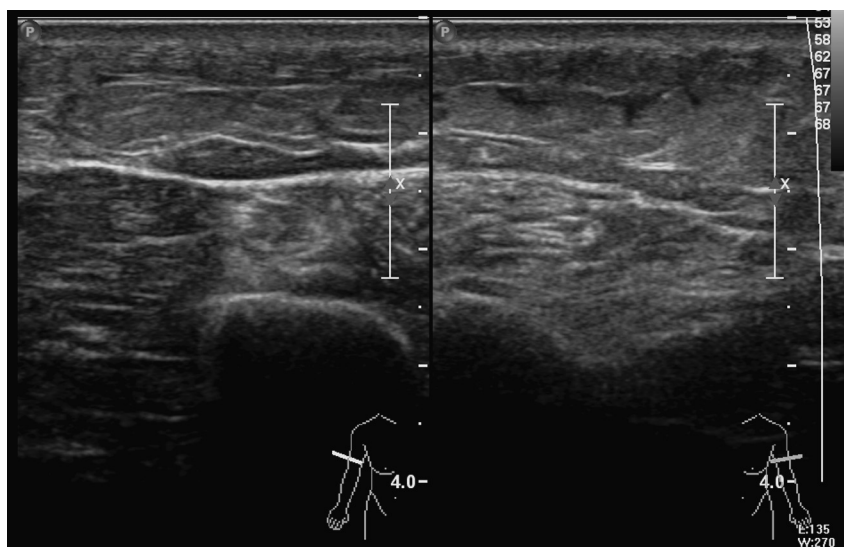


Figure 2 Imaging of this patient. Diffuse edema of subcutaneous and fascia layers of bilateral upper arms by ultrasonography.



Figure 3 Edema with hyperintensity of the muscles and subcutaneous regions of bilateral upper extremities by magnetic resonance imaging (coronal view, fat-suppressed T2-weighted).

search, no other causes of edema could be identified in our patient, except the active DM. Severe widespread subcutaneous edema or anasarca in association with both juvenile and adult-onset DM has been reported, but only very rarely.

Pathogenesis of generalized edema in DM is unclear, but capillary inflammation with increased vascular permeability has been suggested.⁵ Generalized subcutaneous edema, which denotes a very active inflammation, is perhaps caused by increased capillary permeability and endothelial damage, due to deposition of immune complexes as documented by the presence of vasculitis of small blood vessels and edema of the dermis in skin biopsy.⁸ All patients had improved swelling only after aggressive immunotherapy, a finding which strongly suggested that the edema had a close relation to the pathophysiology of DM.⁹

The clinical features of the 14 reported cases of DM associated with generalized edema^{1–10} and the present case are summarized in Table 1. Altogether, there are 10 females and 5 males, with ages ranging from 23 years to 78 years (mean = 49.7 years), a finding consistent with the female predominance in adult patients with DM. Edema affects the limbs, trunk, and face in various combinations and usually begins early in the course of the disease (< 10 weeks) in most patients. A highly active

disease, with pronounced muscle weakness and dysphagia, or esophageal involvement, is another characteristic of this variant.⁵ Significant dysphagia, noted in the 10 previously reported cases, often appears concomitantly with the resolution of edema and a decline in serum muscle enzyme levels.⁶ However, our patient suffered from dysphagia prior to the resolution of edema, and the dysphagia continued despite the normalization of muscle enzyme levels and gradual improvement of proximal muscle strength.

Although most of the patients initially presented with a very active disease, its prognosis seems to be relatively good (Table 1). Only one patient died⁵; the other patients eventually had resolution of anasarca after immunosuppressant therapy. One case recovered, without any treatment.³

Treatment of DM associated with generalized edema varied. Most patients' symptoms responded to a systemic corticosteroid, followed by methotrexate, intravenous immunoglobulin (IVIG), azathioprine, cyclosporine, and mycophenolate mofetil (Table 1). Glucocorticoids can decrease the severity of edema through potent anti-inflammatory and immunosuppressive effects.⁷ Chai et al⁹ reported the lack of significant improvement with corticosteroids alone, and more aggressive immunotherapy, including methotrexate and IVIG, was required. IVIG has been shown to be effective in a case resistant to corticosteroids, azathioprine, and mycophenolate mofetil, and also in patients with bulbar involvement.⁸ IVIG therapy, however, was not effective in some cases; one such case responded to intravenous pulse methylprednisolone, followed by high dose oral prednisolone.⁷ Rituximab has been used to treat refractory inflammatory myopathies.¹⁵ Its therapeutic effect in DM associated with generalized edema is unknown, but it may be considered as an alternative for the refractory cases.⁷

In treatment-refractory cases, it is also noteworthy to consider a positron emission tomography (PET) scan to exclude underlying malignant diseases, as illustrated in the case reported by Haroon et al.⁸ The patient's muscle weakness and edema were resistant to corticosteroids, azathioprine, and mycophenolate mofetil. Her initial malignancy screen was negative, but a PET scan revealed a cervical tumor along with a suspected metastatic lung nodule. The refractory DM was brought under control after the tumors were treated.⁸

In the present case, the muscle weakness and generalized edema showed a good, but transient improvement to oral dexamethasone initially, which was soon followed by a marked worsening of the muscle weakness with edema and disabling dysphagia

Table 1 Characteristics of 15 patients with edema associated with adult dermatomyositis.

Authors ^{Ref}	Sex	Age (y)	Disease duration (wk)	Predominant site of edema	Dysphagia	Treatment	Associated internal malignancy	Outcome
Nitsche ¹	F	62	20	Upper limbs, trunk	+	CS	N/A	Recovered
Smyth et al ²	F	27	4	Forearms	–	CS, AZA	–	Recovered
Gorelik et al ³	M	31	2	Upper-lower limbs	+	CS, IVIG	–	Recovered
Gorelik et al ³	M	63	2	Left arm	–	None	–	Recovered
Mroue et al ⁴	F	78	1	Upper limbs	–	CS	–	Recovered
Werner de Castro et al ⁵	M	40	56	Upper-lower limbs, trunk	+	CS, IVIG	–	Died
Ito et al ⁶	F	78	1.4	Upper-lower limbs	+	CS	–	Recovered
Lee et al ⁷	F	48	4	Face, upper-lower limbs	+	CS, MTX, IVIG, CPT	–	Recovered
Haroon et al ⁸	F	61	1	Face, upper-lower limbs, trunk	+	CS, AZA, MMF, IVIG	Cervical cancer	Recovered
Chai et al ⁹	M	62	8	Upper-lower limbs	+	CS, MTX, IVIG	N/A	Recovered
Chai et al ⁹	F	23	16	Upper-lower limbs	–	CS, MTX, IVIG	N/A	Recovered
Chai et al ⁹	F	38	12	Lower limbs	+	CS, MTX, IVIG	N/A	Recovered
Chai et al ⁹	M	38	N/A	Upper limbs	+	CS, MTX, IVIG	N/A	Recovered
Jung et al ¹⁰	F	52	40	Upper-lower limbs, trunk	+	CS, IVIG, AZA, CYC	–	Recovered
Our patient	F	44	8	Face, upper limbs	+	CS, CPT	–	Recovered

AZA = azathioprine; CPT = corticosteroid pulse therapy; CS = corticosteroids; CYC = cyclosporine; F = female; IVIG = intravenous immunoglobulin; M = male; MMF = mycophenolate mofetil; MTX = methotrexate; N/A = not available.

that eventually required methylprednisolone pulse therapy. Myasthenia gravis was considered as a potential cause for the patient's severe bulbar involvement and poor response to corticosteroids. However, it was excluded by normal responses in a repetitive nerve stimulation test and a negative neostigmine diagnostic test. Alternative treatments, such as methotrexate, azathioprine, or IVIG, were not prescribed to our patient, due to elevated hepatic enzymes, a slower-onset of action, or not being covered by health insurance, respectively.

In conclusion, generalized subcutaneous edema is a very rare manifestation of DM that can occur as a presenting symptom. It may be a hallmark of a severe form of DM that requires prompt and aggressive treatment. The clinical course of generalized edema varies, and early recognition is essential for better disease control. Additional cases are needed to establish guidelines for treatment of this rare variant.

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